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July 16, 2004

Via Facsimile

Assistant Commissioner for Patents
Washington, D.C. 20231

Re: United States Patent Application
For: METHOD FOR IMPROVING TREATMENT SELECTIVITY AND EFFICACY USING INTRAVASCULAR PHOTODYNAMIC THERAPY
Serial No.: 09/871,441
Our Reference Nos.: C017858/0120103

Sir:

We are enclosing papers for the above-referenced patent application. The papers are:

1. Transmittal letter (1 page, in duplicate);
2. Response to Office Action; and,
3. Interview Summary.

It is our understanding that no fee is required; however, if we are mistaken, please charge any fee to Deposit Account No. 02-4467.

Kindly date-stamp and return the enclosed self-addressed, stamped postcard.

Respectfully submitted,

Roxana Wizorek

RW:lcm
Enclosures

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Docket No.: C17858/120103

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

STEVEN J. RYCHNOVSKY

OFFICIAL

Serial No.: 09/871,441

Filed: May 31, 2001

For: METHOD FOR IMPROVING TREATMENT SELECTIVITY AND EFFICACY USING INTRAVASCULAR PHOTODYNAMIC THERAPY

Examiner: R. Henley, III

Art Unit: 1614

Assistant Commissioner for Patents
Washington, D.C. 20231

Response to Office Action

In the Office Action mailed April 16, 2004, the Examiner rejected claims 1-55 and 57-60 under 35 U.S.C. § 103(a) as being unpatentable over Lamuraglia (WO 01/24825 A2).

Applicant respectfully submits that the Lamuraglia reference does not teach or suggest all the limitations of Claims 1-55 and 57-60. Furthermore, based on the teachings of Lamuraglia, one skilled in the art would neither consider utilizing short wavelengths of light to excite a photosensitizer drug, nor appreciate the benefits of using short wavelengths of light for this purpose.

In its application, Applicant discloses the concept of using wavelengths in the range of about 390 nm to 610 nm to excite photosensitizers in cardiovascular applications of photodynamic therapy. The feasibility of this concept was supported by data included in the application that showed this approach provided a means of delivering a selective treatment to the vessel wall. Applicant also presented data in the application showing that excitation using longer wavelengths (greater than 610 nm) did not provide a selective or efficacious response. Instead,

Applicant showed that use of such longer wavelengths resulted in significant damage to surrounding tissues. This result was unexpected since the prior art had taught the opposite approach, i.e. the prior art, including LaMuraglia, teaches the advantages of using longer wavelengths (greater than 610 nm) and the disadvantage of using wavelengths shorter than 610 nm.

The primary reason for the use of wavelengths longer than 610 nm, as expressed in the prior art, was to avoid the absorption of light by blood. This view is documented in the references Applicant provided with the original application, including that of LaMuraglia. While blood absorbs at all visible wavelengths, it absorbs particularly strongly at wavelengths less than 610 nm. Consequently, the prior art taught that wavelengths longer than 610 nm should be used in order to avoid this absorption.

A summary of these absorption characteristics was included in our amendment submitted on November, 7 2003. See Response to Office Action dated November 7, 2003 at pg. 3. In response to the Examining Attorney's request during the July 8, 2004 interview, this response to Office Action further clarifies these effects, particularly the manner in which blood affects the penetration of light through tissue.

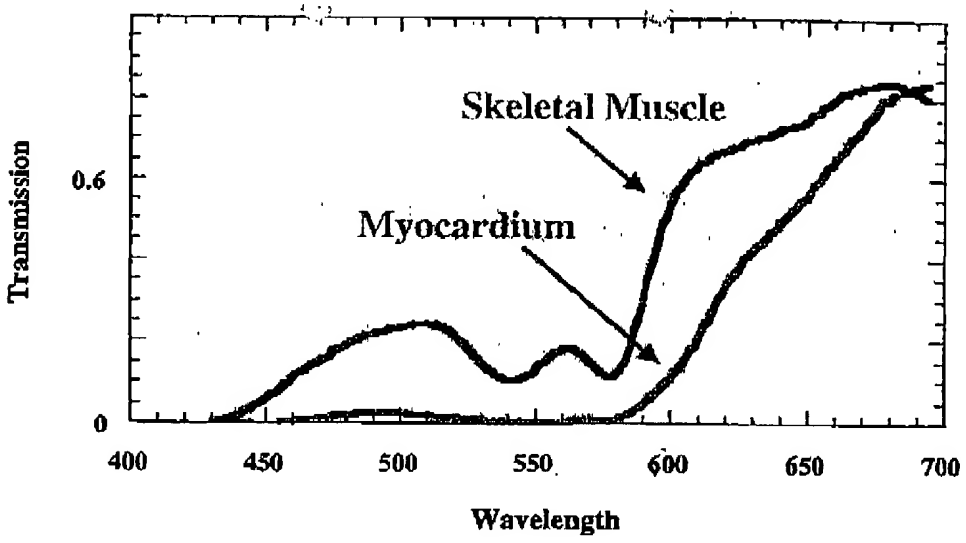
In Applicant's original application, Applicant provided data showing that when an endovascular light source was used (which is what would be used in practice), wavelengths in the approximate range of 610 nm and greater led to significant damage to surrounding tissues, while shorter wavelengths did not. See Application at pg. 8, lns. 21-23, pg. 14, lns. 10-17, Figs. 1-3, 9. Furthermore, Applicant found that it could not achieve efficacy with an endovascular light source when using wavelengths in the approximate range of 610 nm and greater but did achieve efficacy when using shorter wavelengths. Applicant believes this is most likely the result of two factors.

First, it is well known that light scattering in tissue increases as the wavelength decreases. This will cause shorter wavelength light to be more strongly scattered and consequently it

will be more concentrated within the vessel wall instead of in surrounding tissue. See Application at pg. 14, lns. 22-23.

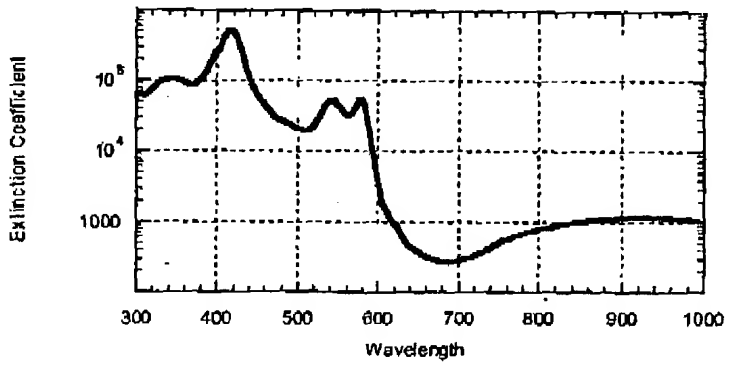
Second, blood absorption increases significantly when the wavelength drops below 610 nm. This absorption will prevent such wavelengths from penetrating as deeply as longer wavelengths. See Application at pg. 14, lns. 22-23. Previous to completing Applicant's experiments Applicant did not realize that light confinement was critical. Rather, based on the prior art, Applicant believed the opposite to be true.

The significance of the 610 nm wavelength threshold can be seen in a measurement of the transmission of light through tissue over a range of wavelengths. This data is presented as Figure 13 of our original patent application and duplicated below:

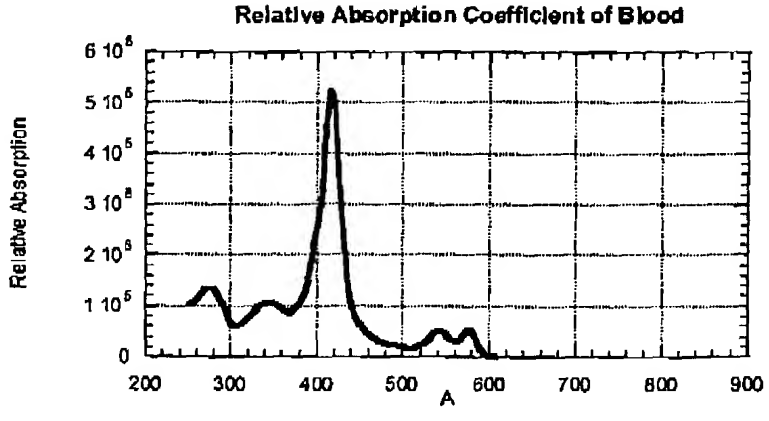


In Figure 13, Applicant shows that for myocardium tissue (which is highly perfused with blood and contains high levels of myoglobin) there is very little transmission of light through the sample thickness shown, at least for wavelengths less than approximately 610 nm. Also, for the skeletal muscle, (which is less perfused with blood), there is a gradual decrease in light transmission as

wavelength is decreased. However, at approximately 610 nm the slope of this line increases significantly from a gradual slope to a much steeper slope. This is an indication of the onset of absorption from a different absorbing species. In fact, as a result of this increased absorption, a thicker sample than shown here would transmit very little light for wavelengths shorter than 610 nm. Furthermore, as evidenced by the two transmission nulls at approximately 540 nm and 580 nm, this absorption of light is significantly influenced by the hemoglobin in these tissues. Figure 11 of the application (reproduced below), shows the absorption peaks in hemoglobin at 540 nm and 580 nm:



This is also supported by the following chart also included in Applicants November amendment:



Although Applicant attributes the unexpected results seen in its experiments to be in part due to a hemoglobin related drop in transmission at 610 nm, the exact absorbing species responsible for this effect may not be important. The significance of Applicant's disclosure is that, contrary to the prior art, wavelengths longer than approximately 610 nm are not practical for use in cardiovascular photodynamic therapy. Furthermore, again contrary to the prior art, wavelengths shorter than 610 nm are practical and preferable for use in cardiovascular photodynamic therapy. In effect the absorbing species in the tissue (most likely hemoglobin) helps to protect critical tissues from inadvertent treatment. Apparently, the prior art did not view this characteristic to be useful and apparently viewed it to be unnecessary and perhaps undesirable. We have found the opposite to be true.

Therefore, the methods claimed in the present application are patentably distinct from the methods discussed in the prior art, including Lamuraglia, and furthermore, based on the teachings of the prior art, one skilled in the art would neither consider utilizing short wavelengths or light to excite a photosensitizer, nor appreciate the benefits of using short wavelengths for this purpose. In fact as stated in section M.P.E.P. § 2144.05, a prima facie case of obviousness based on alleged over lapping ranges may be rebutted by showing: (1) "the criticality of the claimed range," as Applicant has demonstrated with respect to wavelengths shorter than 610 nm; or (2) that "the art, in any material respect, teaches away from the claim invention," as Applicant has demonstrated that the Lamuraglia reference advocates the use of long wavelengths to avoid blood absorption of light, see Lamuraglia, WO 01/24825 at p. 6 ("MB has a maximum light absorption at 660 nm, which allows deep and homogeneous tissue penetration by light which is unaffected by blood."); Lamuraglia, WO 01/24825 at p. 10 (preferred range "from about 680 and about 700 nm to avoid blood

absorption, preferably between about 625 nm and about 690 nm, and most preferably about 690 nm for BPD and about 660 nm for MB) (emphasis added).

In light of the foregoing response, reconsideration and withdrawal of the rejection based upon the Lamuraglia reference are respectfully requested.

Respectfully submitted,

By: _____

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